

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 5fpo-01-08	FOR FURTHER ACTION	See item 4 below
International application No. PCT/KR2005/000188	International filing date (<i>day/month/year</i>) 20 January 2005 (20.01.2005)	Priority date (<i>day/month/year</i>) 20 January 2004 (20.01.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant KOREA RESEARCH INSTITUTE OF BIOSCIENCE AND BIOTECHNOLOGY		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a).																								
2.	This REPORT consists of a total of 5 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 40%;">Box No. I</td> <td style="width: 50%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 2px;">Date of issuance of this report 24 July 2006 (24.07.2006)</td> </tr> <tr> <td style="padding: 2px;"> Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Philippe Becamel</div> </td> </tr> <tr> <td style="padding: 2px;">e-mail: pt12@wipo.int</td> </tr> </table>	Date of issuance of this report 24 July 2006 (24.07.2006)	Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Philippe Becamel</div>	e-mail: pt12@wipo.int
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Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Philippe Becamel</div>				
e-mail: pt12@wipo.int				

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PCT/KR2005/000188

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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Seoul 135-080 Republic of Korea

28/7

PCT

REC'D 31 MAY 2005

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) 20 MAY 2005 (20.05.2005)Applicant's or agent's file reference
5fpo-01-08

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/KR2005/000188

International filing date (day/month/year)

20 JANUARY 2005 (20.01.2005)

Priority date(day/month/year)

20 JANUARY 2004 (20.01.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC7 C12N 15/12

Applicant

KOREA RESEARCH INSTITUTE OF BIOSCIENCE AND BIOTECHNOLOGY et al

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/KR



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Telephone No. 82-42-481-8132



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/KR2005/000188

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☒ in written format
☒ in computer readable form

c. time of filing/furnishing

- ☒ contained in the international application as filed.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/KR2005/000188

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-7	YES
	Claims	None	NO
Inventive step (IS)	Claims	1-7	YES
	Claims	None	NO
Industrial applicability (IA)	Claims	1-7	YES
	Claims	None	NO

2. Citations and explanations :

The following documents have been considered for the purpose of this written opinion:

- D1: Blood, Vol. 100(1), pp. 89-95 (2002)
- D2: Curr. Top. Dev. Biol., Vol. 50, pp. 45-60 (2000)
- D3: Blood, Vol. 93(4), pp. 1168-1177 (1999)
- D4: Genes & Dev., Vol. 13(9), pp. 1073-1078 (1999)
- D5: Oncogene, Vol. 18(13), pp. 2181-2188 (1999)

D1 discloses a human Mix-like homeobox gene expression restricted to immature B and T cells. D1 generally mentions that the gene may be involved in hematopoietic fate through the SCL regulation, which is one of the factor required for the differentiation of uncommitted hematopoietic progenitors with high precision. The assumption is based on the fact that the Xenopus Mix.1 induces expression of Xenopus SCL.

D2 also discloses the involvement of the members of the Mix of homeobox transcription factor in the induction of ventral mesoderm, where the formation of hematopoietic stem cells during development occurs.

D3 discloses the Gata2 and Myb genes correlated with the potential of the $\alpha 4$ -integrin+ cells to give rise to hematopoietic cell differentiation, which is the molecule expressed on a hematopoietic stem cell.

D4 reveals the importance of the c-Myb transcription factor for fetal hematopoiesis and early stages of T-cell development by studying transgenic null mice.

D5 discloses that the oncoproteins c-Myc and E1A render cells vulnerable to NK cell mediated cytotoxicity, which means the activation of the function of NK cells.

(Continued on Supplemental Sheet.)

**WRITTEN OPINION OF THE
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PCT/KR2005/000188

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box No. V

I. Novelty

The present invention relates to a composition containing a gene regulating differentiation from stem cells into natural killer cells as an effective ingredient. Even though the prior art documents disclose the suggestive result which is related to the involvement of those genes in hematopoietic lineage, none of the prior art documents disclose that they directly regulate differentiation from stem cells into natural killer cells.

Therefore, the subject matter of claims 1-7 is considered to be novel under PCT Article 33(2).

II. Inventive Step

D1 and D2 suggest the Mix-like homeobox gene regulates the SCL expression, which is the factor for patterning the mesoderm during gastrulation. But this stage for patterning the mesoderm is too broad for the man skilled in the art to anticipate the role of a Mix-like homeobox gene differentiating the hematopoietic stem cell into the NK cell.

D3 and D4 also designate the role of c-Myb to determine the fate of the endothelial progenitors to the earliest precursor of hematopoietic cell lineage, not the differentiation of the NK cell diverged from the stem cell, which is the main function of the composition of this invention.

In D5, the c-Myc activates the NK cell induced cytotoxicity at a post-triggering stage of NK cell-target cell interaction. The activation of NK cell induced cytotoxicity is related to the function of a mature NK cell. The subject matter of this invention differs from the teaching of D5 in that the c-Myc regulates the differentiation into a mature NK cell. The skilled person cannot anticipate the role of c-Myc for the differentiation into the mature NK cell, out of the NK cell induced cytotoxicity as disclosed in D5.

Therefore, the subject matter of this invention seems to involve an inventive step under PCT Article 33(3).

III. Industrial Applicability

The subject matter of claims 1-7 is considered to be industrially applicable under PCT Article 33(4).

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